SYNTHESIS OF NITROGENOUS COMPOUNDS

DISSERTATION SUBMITTED
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE AWARD OF THE DEGREE OF

Master of Philosophy

IN

CHEMISTRY

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BY

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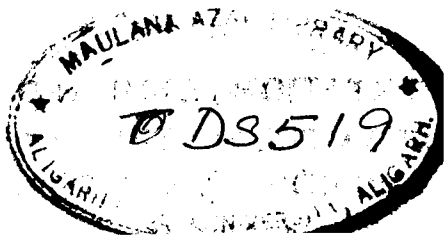
DEPARTMENT OF CHEMISTRY
ALIGARH MUSLIM UNIVERSITY
ALIGARH

1983



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The dissertation entitled, 'Synthesis of Some Nitrogenous compounds' by Mr. Mashkoor Husain in partial fulfilment of his Master of Philosophy degree is suitable for submission.

(N.H. Khan)
Reader in Chemistry

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Mashkoor Husain

(MASHKOOR HUSAIN)

CONTENTS

THEORETICAL

REACTIONS OF PHOSGENE

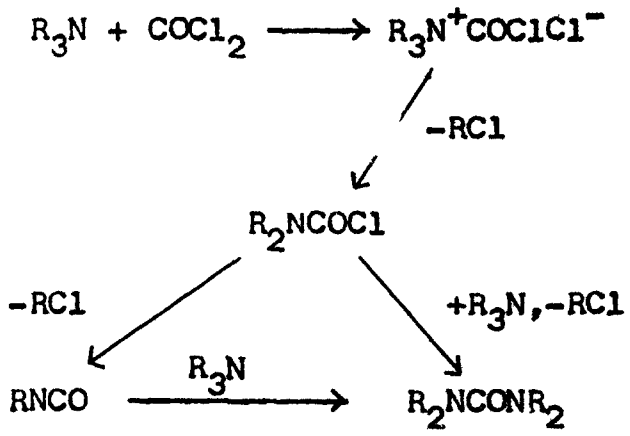
Phosgene is a binding block for the synthesis of a wide variety of organic compounds and it has been used as a reagent for carbonylation, chlorination and dehydration. In the following pages different modes of reactions of phosgene are described.

REACTIONS OF PHOSGENE AT THE NITROGEN CENTRE

The most widely documented aspect of phosgene chemistry is the interaction of the reagent with a nitrogen centre. In such reactions, phosgene initially reacts with the nitrogen lone pair to form an intermediate complex which collapses, with the elimination of RCl, to give a stable carbamoyl chloride derivative. The carbamoyl chloride thus formed can eliminate RCl to create a new site of unsaturation and/or react further with another molecule of starting material to afford urea derivatives (Scheme-1). These secondary reactions are, for the most part beyond the scope of the present dissertation.

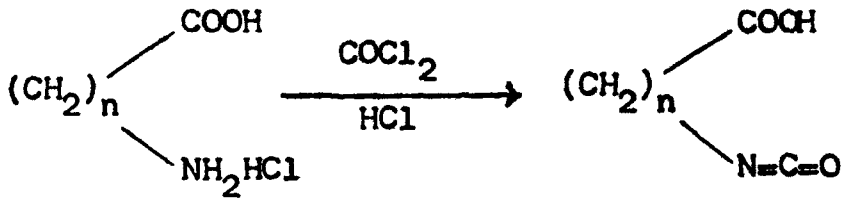
The reactivity of phosgene with nitrogen compounds is typical of the reactivity of acyl halides, in general and can be ordered by conventional electronic and steric considerations. The availability of the nitrogen electron pair for bonding and the steric environment about the centre determine the reactivity of the various nitrogenous functional groups.

Scheme-1



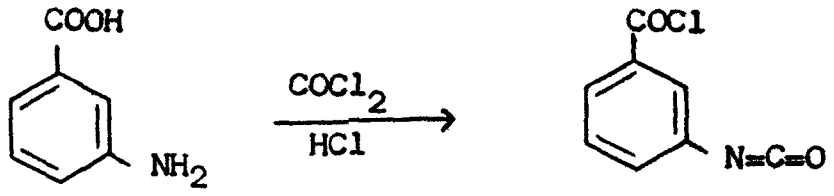
The reaction of phosgene at nitrogen and at other suitable sites has been described in a number of reviews but our discussion will be confined to some selected novel contribution which have appeared in the literature.

Iwakura et al.[1] reported the formation of isocyanate acid chlorides (II and IV) by the reaction of amino acid hydrochlorides (I and III) with phosgene in the presence of HCl.



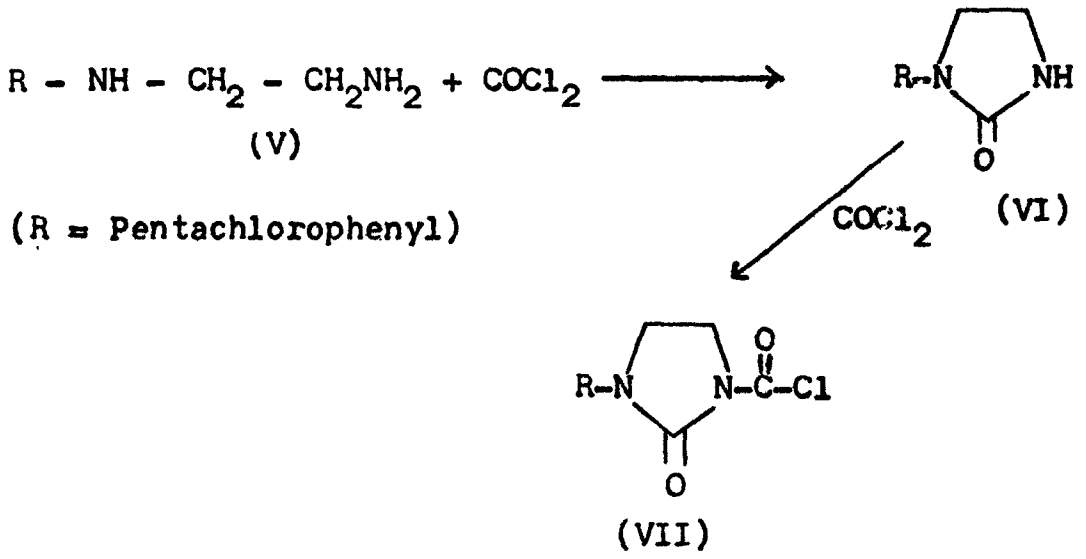
(I) (II)

(n = 2,4)

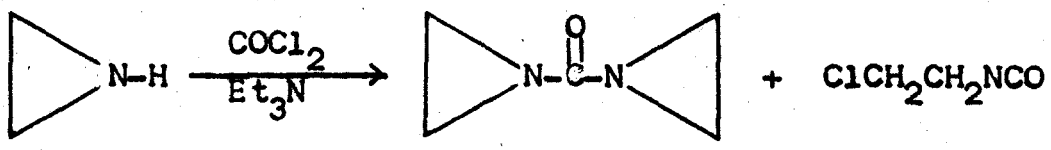


(III) (IV)

Treatment of ethylene diamine or its derivatives (V) with phosgene has been reported to afford cyclic ureas (VI)[2] which readily convert to allophonylchloride derivatives (VII).

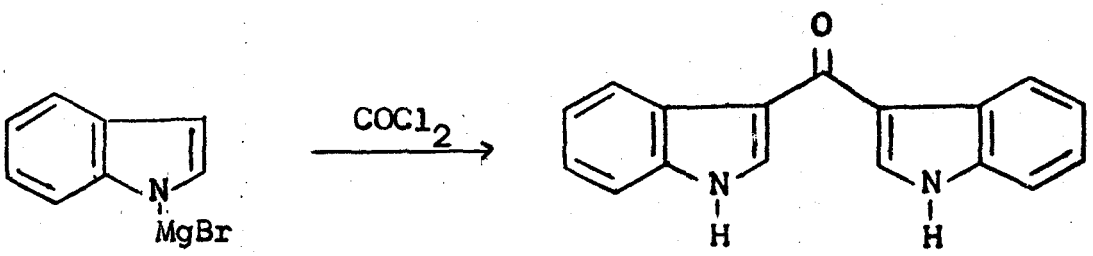


Tomalia and Paige[3] when treated equivalent amounts of aziridine (VIII) and triethylamine in carbon tetrachloride containing 1 equivalent of phosgene at -10°, obtained a mixture of bisaziridinylurea (IX) and 2-chloroethyl isocyanate (X), the former being the major product.

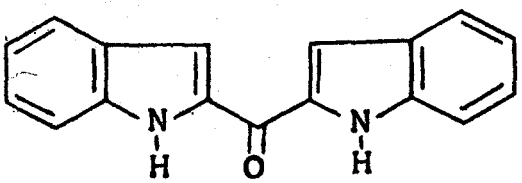


(VIII) (IX) (X)

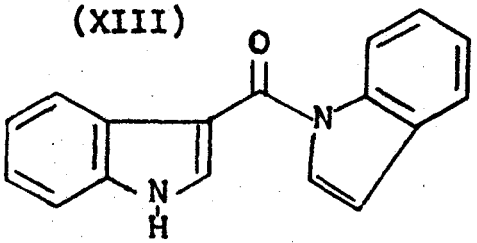
The reaction of indole magnesium bromide (XI) with phosgene was first reported by Oddo and Mingoia[4]. They have shown the formation of several carbonyl dimeric indoles (XII-XIV).



(XI) (XII)

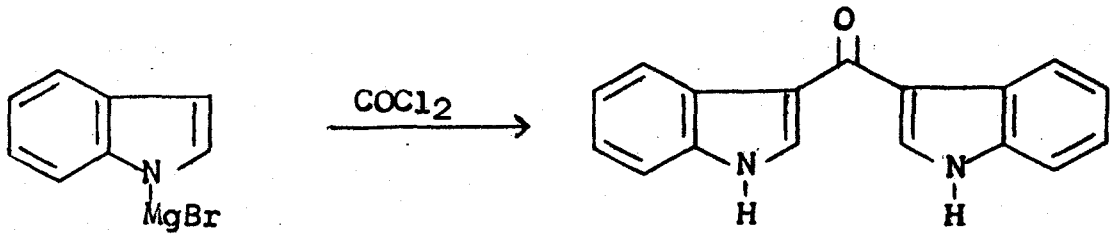


(XIII)

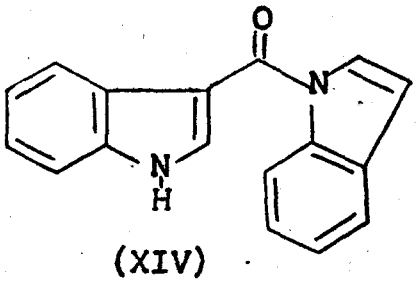


(XIV)

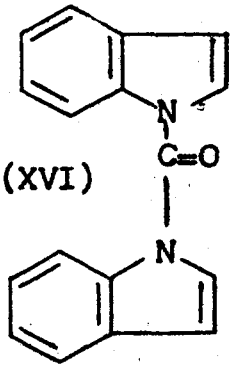
Recently, Bergman et al.[5] have reported carbonyl polymeric derivatives of indole (XII, XIV-XVII) by the reaction of indole magnesium bromide (XI) with phosgene in ether.



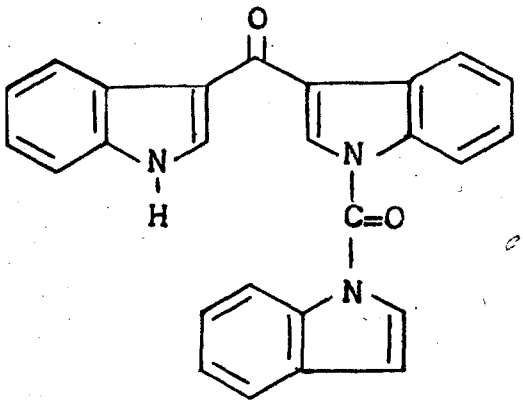
(XI) (XII)



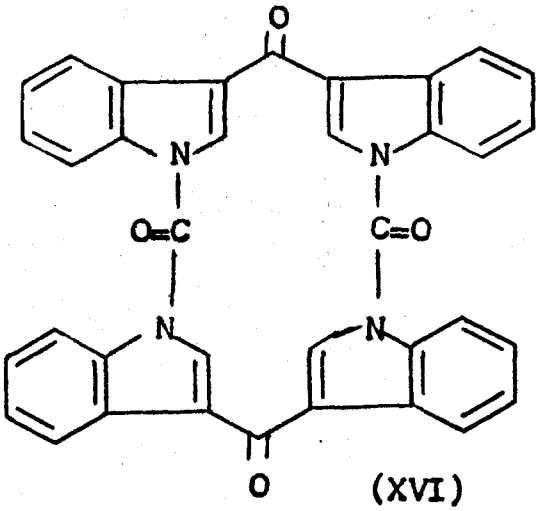
(XIV)



(XVI)

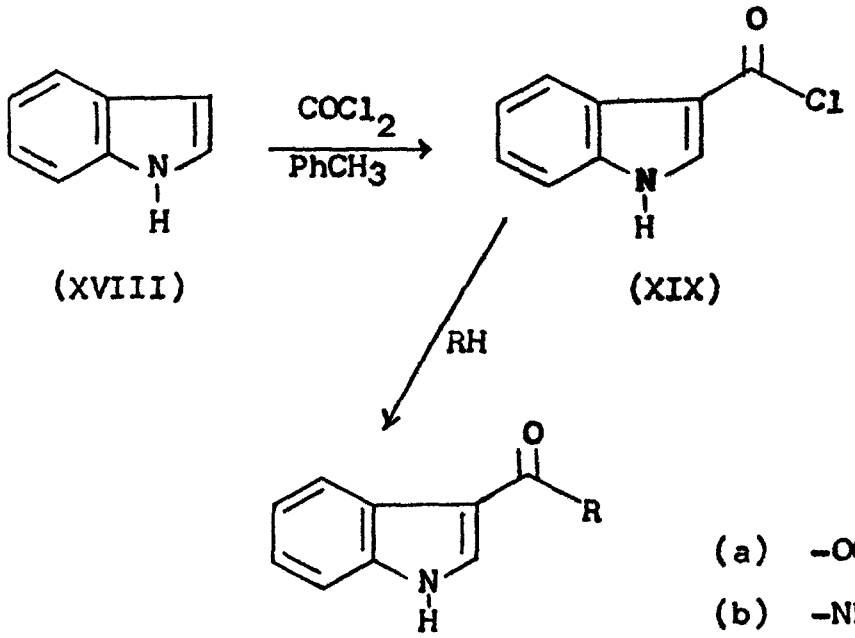


(XVII)



(XVI)

They have also synthesised 3-indole carbonyl chloride (XIX)[5] by the action of phosgene on indole (XVIII) in toluene. From this compound, they obtained a number of derivatives (XXa-e) by replacing chlorine with different nucleophiles.



(XVIII) (XIX) (XX)

R

(a) $-OC_2H_5$

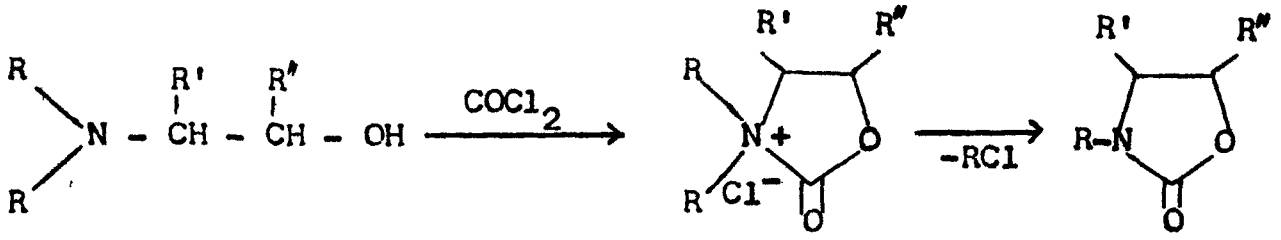
(b) $-NH_2$

(c) $-N(CH_3)_2$

(d) $-NH-NH_2$

(e) $-OH$

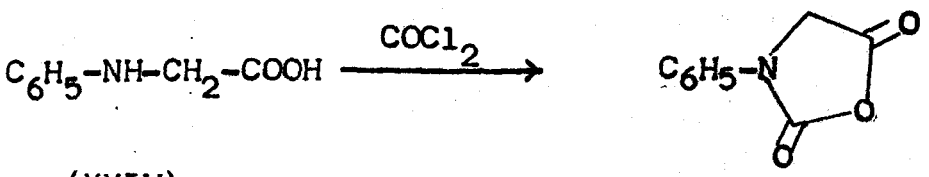
Murdock[6] has shown the formation of 2-oxazolidinone derivatives (XXII and XXIII) by the reaction of phosgene on 2-dialkylamino alkanols (XXI) using pyridine as an acid acceptor.



(XXI) (XXII) (XXIII)

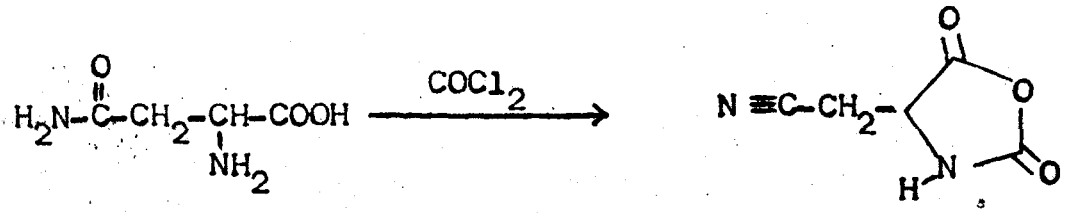
	R	R'=R''
(a)	$-CH_3$	$-CH_3$
(b)	$-CH_3$	$-C_2H_5$
(c)	$-CH_3$	$-C_3H_7$
(d)	$-C_2H_5$	$-CH_3$
(e)	$-C_2H_5$	$-C_2H_5$
(f)	$-C_2H_5$	$-C_3H_7$

Introduction of phosgene into cold alkaline solution of N-phenylglycine (XXIV) has been found[7] to produce N-carboxy anhydride (XXV).



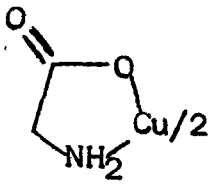
(XXIV) (XXV)

Wilcheck et al.[8] have reported anhydride (XXVII) containing a nitrile group from asparagine (XXVI).

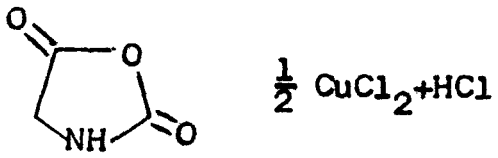


(XXVI) (XXVII)

Preparation of N-carboxyamino acid anhydrides (XXIX) in good yields were reported by Hamilton and Hamilton[9] through the reaction of Cu(II) amino acid complexes (XXVIII) suspended in tetrahydrofuran with phosgene at room temperature.



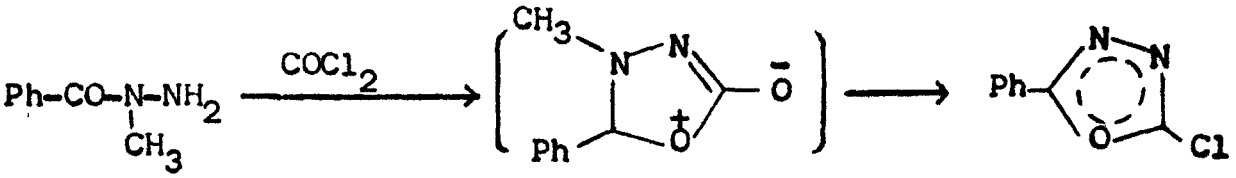
(XXVIII)



(XXIX)

Hydrazine reacts with phosgene to afford good yields of carbohydrazides while acylated derivatives give 1,3,4-oxadiazole derivatives[10].

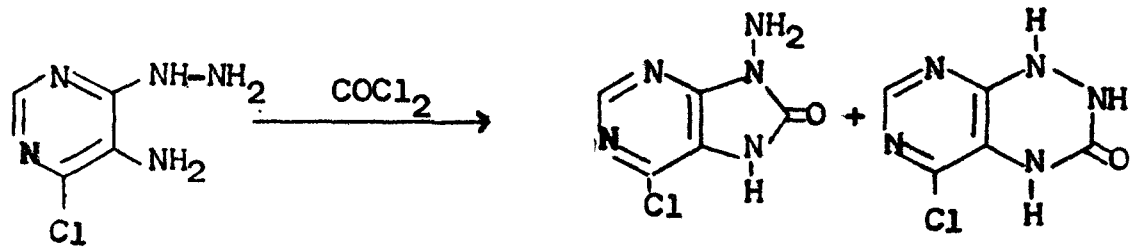
Ainsworth[11] synthesised 2-chloro-5-phenyl-1,3,4-oxadiazole (XXXI) by treating 1-benzoyl-1-methylhydrazine (XXX) with carbonyl chloride.



(XXX)

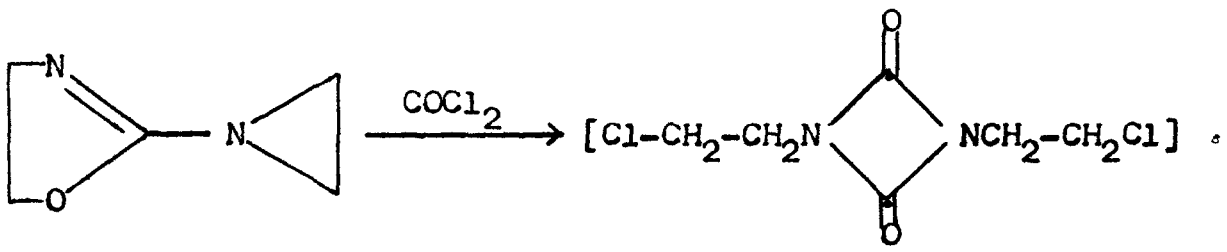
(XXXI)

Krackov and Christensen[12] have reported the formation of purine derivatives (XXXIII and XXXIV) by the reaction of hydrazine derivative, 5-amino-4-chloro-6-hydrazinoperimidine (XXXII) with phosgene.

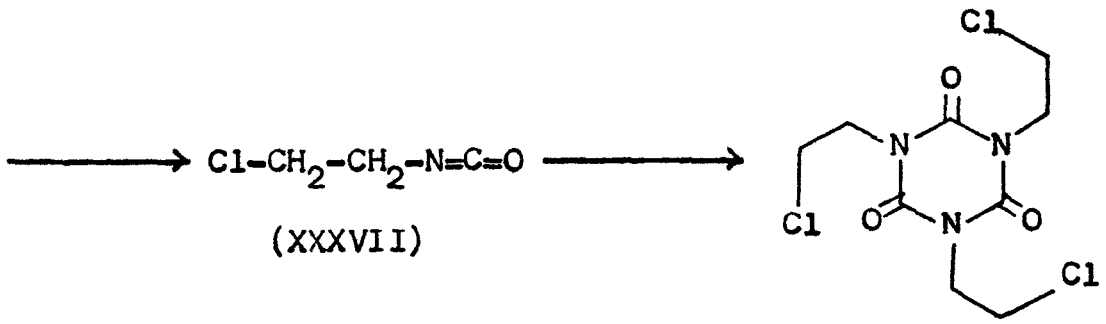


(XXXII) (XXXIII) (XXIV)

Tomalia and co-workers[13] treated 2-aziridinyl-2-oxazoline (XXXV) with phosgene to obtain trimer (XXXVIII) of 2-chloroethyl isocyanate (XXXVII), chloroethyl isocyanate dimer (XXXVI) was postulated to be an intermediate in this reaction.



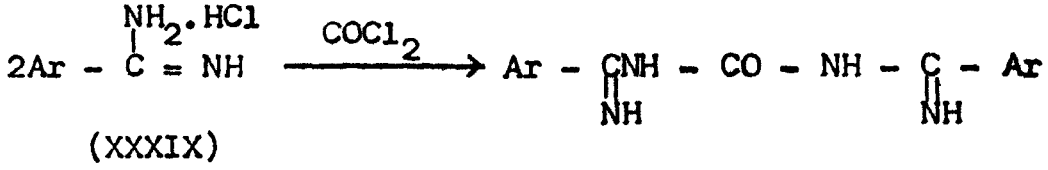
(XXXV) (XXXVI)



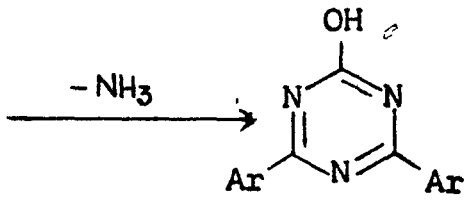
(XXXVII)

(XXXVIII)

It has long been reported[14] that 2,4-diaryl-6-hydroxy-5-triazine (XL) can be prepared by the reaction of 1 mole of phosgene with 2 moles of aryl amidine (XXXIX). The intermediate urea in most cases can be isolated if the reaction is carried out at low temperature.

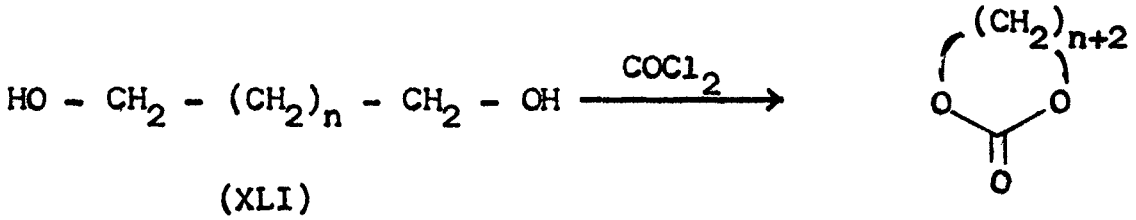


(XXXIX)



(XL)

Sarel et al.[15] have reported the formation of cyclic carbonates (XLII) by treating 1,2-, 1,3- and 1,4-glycols (XLI) with phosgene using an acid acceptor to accelerate the reaction.

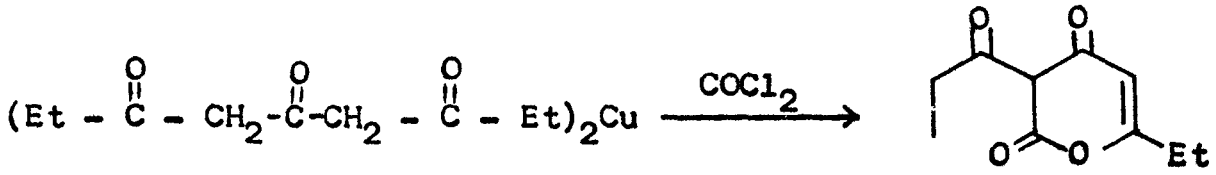


(XLI)

(n = 0, 1, 2)

(XLII)

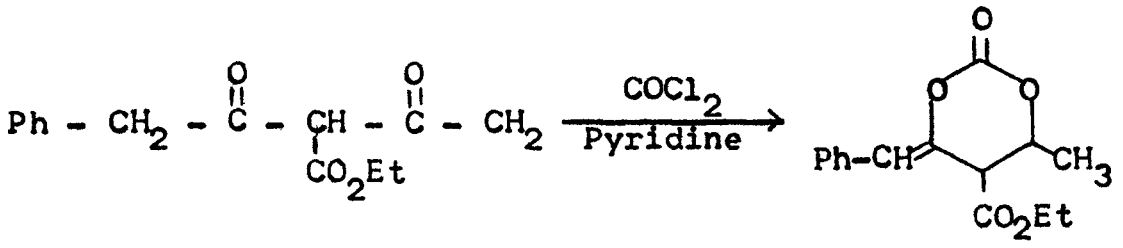
Mohala and Deshpande[16] have synthesised lactone (XLIV) by the reaction of copper salt of 3,5,7-nonanetrione (XLIII) with phosgene. The product is supposed to be formed by the way of an enol chloroformate.



(XLIII)

(XLIV)

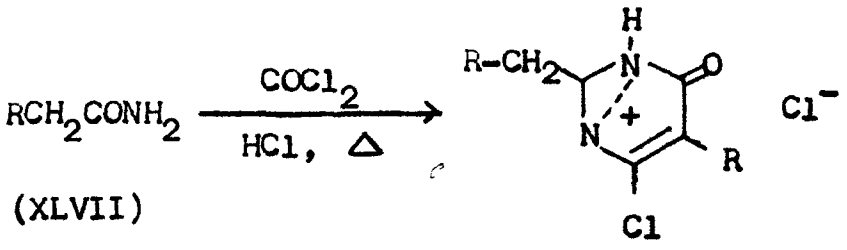
Boltze and Heidenbluth[17] have reported the formation of cyclic carbonates (XLVI) by the reaction of arylacetylaceto acetate (XLV) with phosgene in the presence of pyridine.



(XLV)

(XLVI)

Primary amides (XLVII) when reacted with an excess of phosgene under pressure, furnished pyrimidines (XLVIII)[18].

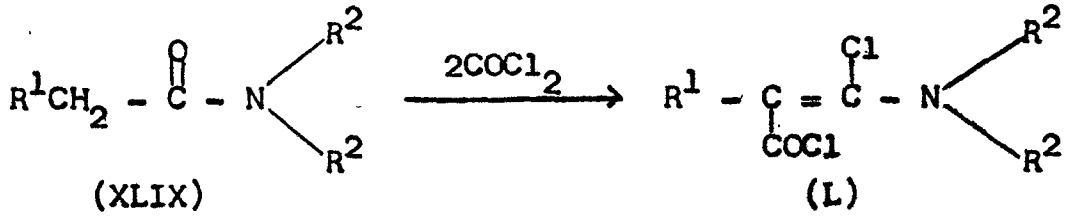


(XLVII)

(R = H, CH_3, C_2H_5)

(XLVIII)

Ulrich et al.[19] obtained α-chloro-β-chlorocarbonyl enamines (L) from the reaction of N,N-disubstituted amides (XLIX) with carbonyl chloride.

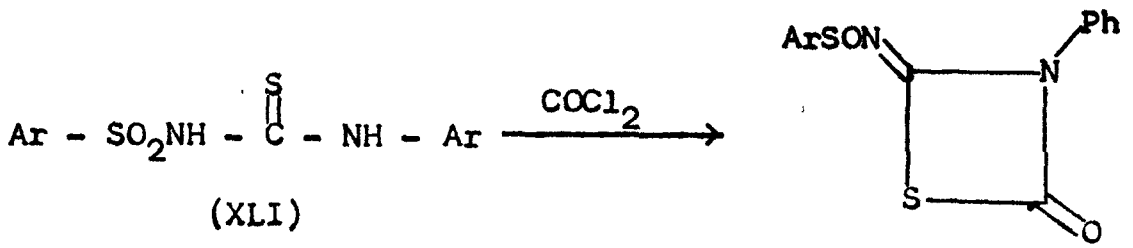


(XLIX)

(L)

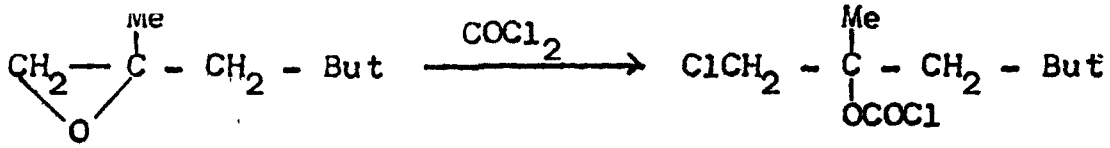
	R^1	R^2
(a)	$-CH_3$	$-CH_3$
(b)	$-CH_3$	$-C_2H_5$
(c)	$-C_2H_5$	$-CH_3$
(d)	$-C_6H_5$	$-C_2H_5$

They have also carried out the synthesis of 1,3-thiazetedine derivative (LII)[20] by treating 1-aryl-3-aryl sulfonyl thiourea (LI) with the reagent.



(XLI) (LII)

Jones[21] subjected epoxide (LIII) to react with the gas ($COCl_2$) and obtained β-chloroformate (LIV). Excess of gas gave the corresponding carbonate.



(LIII) (LIV)

REACTIONS OF PHOSGENE AT THE CARBON CENTRE

Kharasch and Brown[22] have reported the reaction of phosgene with cyclohexane under homolytic conditions giving cyclohexane carbonyl chloride and cyclohexyl chloride. They observe that products formed in the photolysis reaction were dependent on the reaction temperature and proposed the following scheme.

$$COCl_2 + h\nu \longrightarrow Cl^{\bullet} + {}^{\bullet}Cl\text{-}C{=}O$$

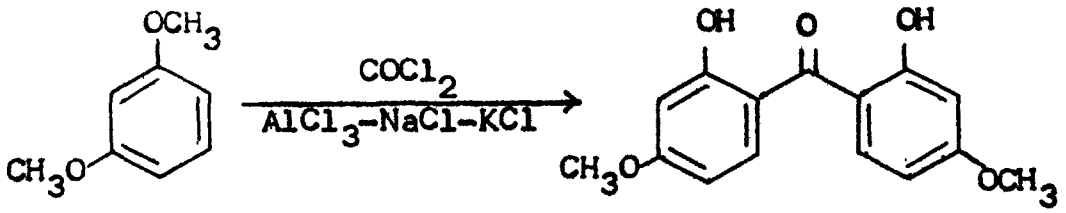
$$C_6H_{12} + Cl^{\bullet} \longrightarrow C_6H_{11}^{\bullet} + HCl$$

$$C_6H_{11}^{\bullet} + COCl_2 \longrightarrow C_6H_{11}COCl + HCl$$

$$ClC{=}O \longrightarrow Cl^{\bullet} + CO$$

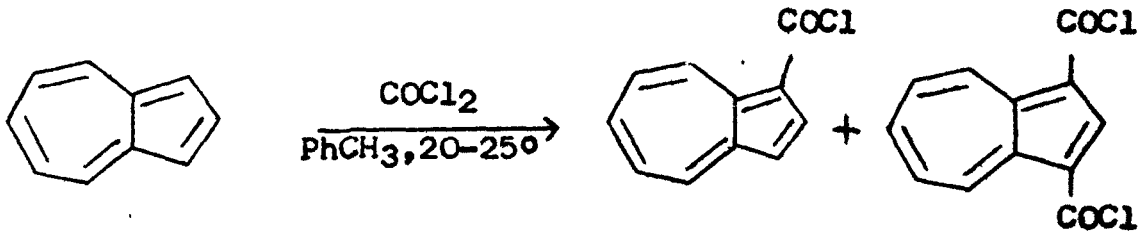
$$C_6H_{11}^{\bullet} + Cl^{\bullet} \longrightarrow C_6H_{11}Cl$$

Triebs and Ortmann[23] have reported the formation of a very interesting product (LVI) by the reaction of 1,3-dimethoxybenzene (LV) with phosgene using $AlCl_3$-NaCl and KCl. In addition to acylation, demethylation also occurred.



(LV) (LVI)

Azulene (LVII) reacts with phosgene even in the absence of Friedel-Crafts catalyst. The reaction occurs at 1 and 3 positions at room temperature to give good yields of azulene carbonyl chlorides (LVIII and LIX)[24].

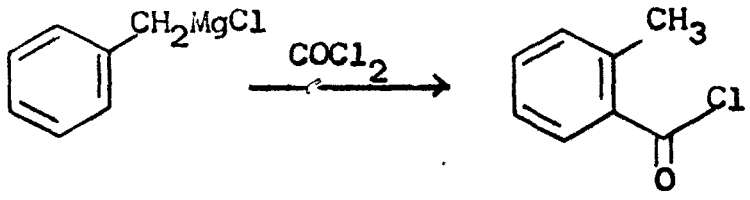


(LVII) (LVIII) (LIX)

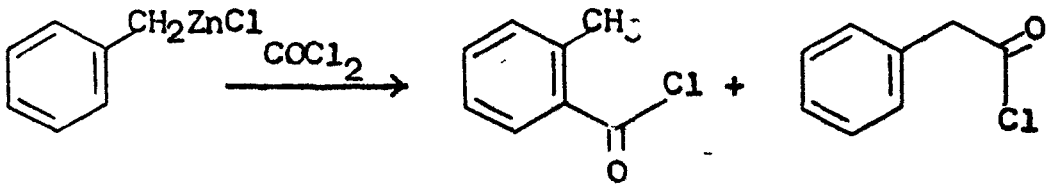
In reaction with alkyllithium[25] phosgene acts as a typical acid chloride, producing carboxylic acids, symmetrical ketones or tertiary alcohols along with dehydration products.

$$C_4H_9Li + COCl_2 \longrightarrow C_4H_9COOH + C_4H_9COC_4H_9 + (C_4H_9)_3C{-}OH + (C_4H_9)_2C{=}CHC_3H_7$$

Jocot-Guillarmod[26] has reported an unusual rearrangement. He treated benzyl Grignard reagent (LX, LXII) with phosgene and obtained ring substituted products (LXI, LXIII and LXIV).

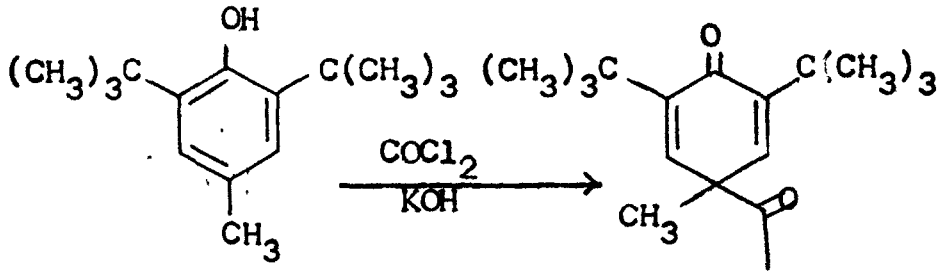


(LX) (LXI)



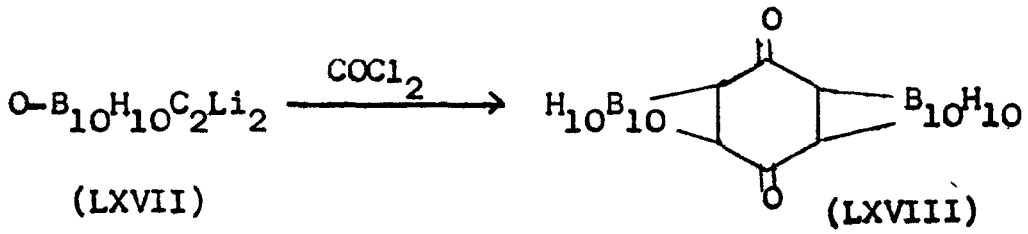
(LXII) ~ 60% (LXIII) ~ 40% (LXIV)

Stansbury Jr. and Cantrell[27] have reported a very interesting acylation. They treated 2,6-di-tert.butyl-4-methyl phenol (LXV) with phosgene in presence of potassium hydroxide. Acylation at the 4 position, instead of chloroformate formation, occurred (LXVI).

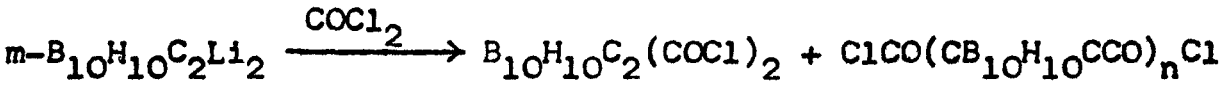


(LXV) (LXVI)

Lithium carboranes[28] (LXVII and LXIX) react with phosgene to give simple carbonyl derivatives of the carborane. Depending on the nature of the starting material both acid chlorides (LXX and LXXI) and ketones (LXVIII) can be formed.

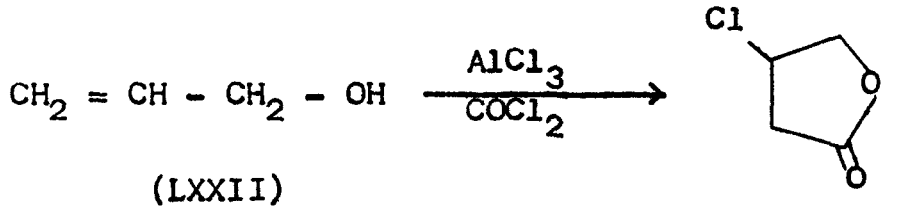


(LXVII) (LXVIII)



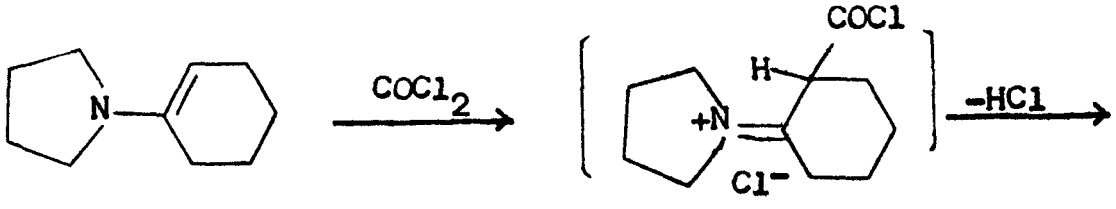
(LXIX) (LXX) (LXXI)

Allyl alcohol (LXXII) reacts with phosgene in the presence of $AlCl_3$ to form β-chlorolactone (LXXIII)[29].

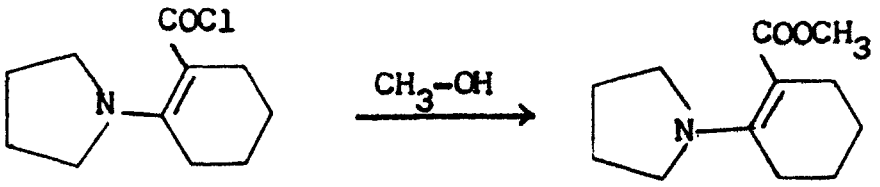


(LXXII) (LXXIII)

Enamine (LXXIV) has been reported[30] to afford chloroformyl enaimine (LXXV), isolated as methyl ester (LXXVI), in the presence of a base.

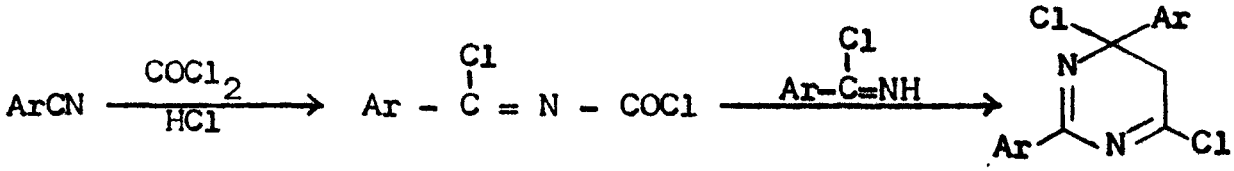


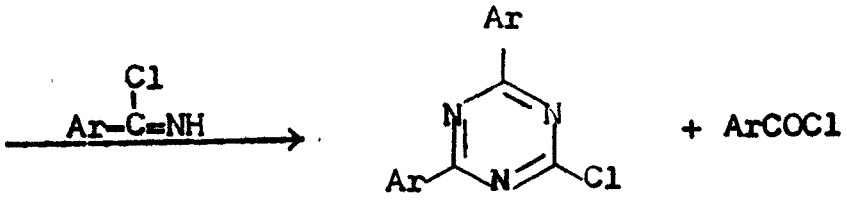
(LXXIV)



(LXXV) (LXXVI)

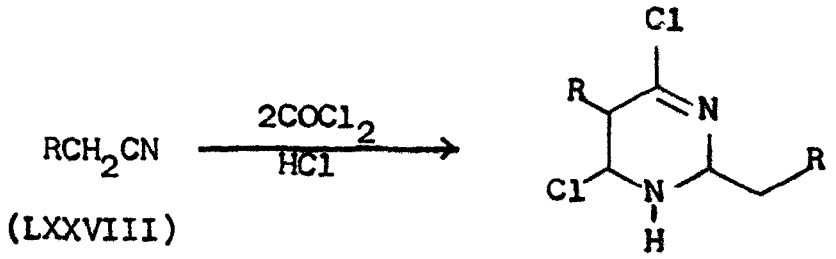
Yanagida et al.[31] treated aryl nitrile with phosgene in the presence of HCl. It yielded 2-chloro-4,6-diaryl-1,3,5-triazine (LXXVII) and benzoyl chloride.





(LXXVII)

Aliphatic nitriles (LXXVIII) having atleast one α-hydrogen atom react with phosgene in the presence of HCl to produce 6-chloro-2,5-dialkyl-4-pyrimidine hydrochlorides[32] (LXXIX).

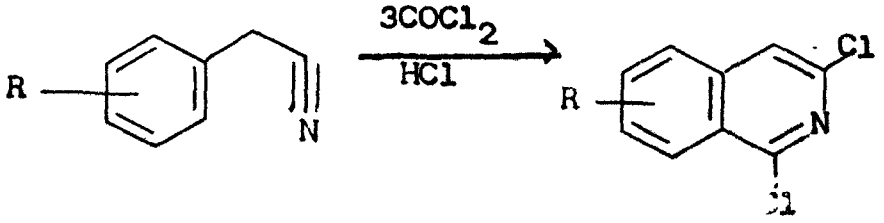


(LXXVIII)

(R = H, CH_3)

(LXXIX)

Arylacetonitriles (LXXX) when treated with an excess of reagent, furnished 1,3-dichloroisoquinolines (LXXXI)[33].



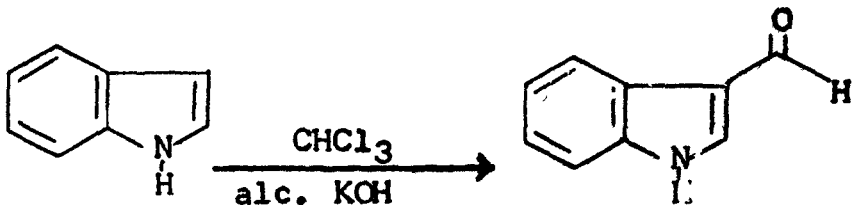
(LXXX)

(LXXXI)

REACTIONS OF INDOLE

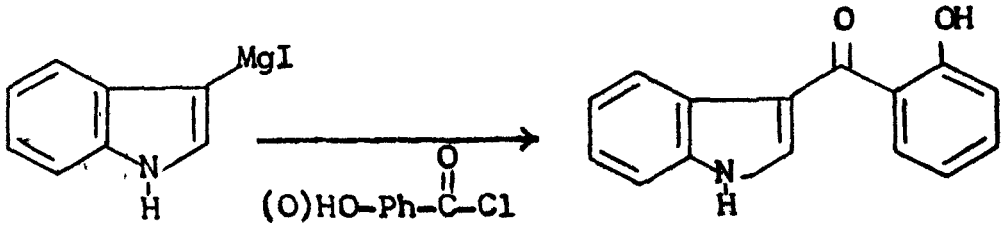
An electrophile when subjected to react with indole, prefers position 3 or 1 because of the high electron density at these centres. Substitution at C3, in accordance with aromatic electrophilic substitution is well known. These reactions at indole and its derivatives have been studied in detail.

Eltinger and Flamond[34] prepared indole-3-aldehyde (LXXXII) by the action of chloroform and alcoholic potassium hydroxide on indole (XVIII).



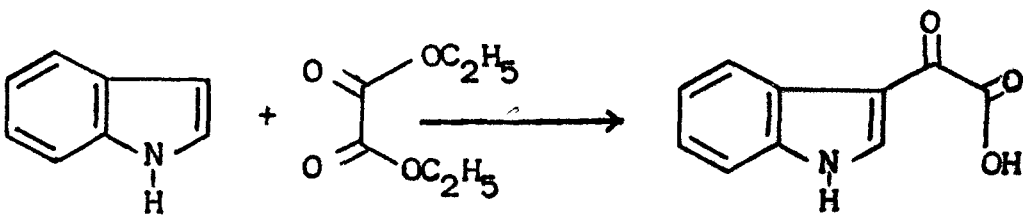
(XVIII) (LXXXII)

Toffoli[35] subjected indolyl magnesium iodide (LXXXIII) to react with salicyl chloride to obtain 3-indolyl-O-hydroxy phenyl ketone (LXXXIV).



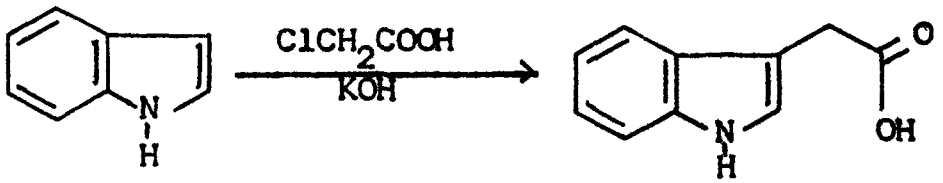
(LXXXIII) (LXXXIV)

Elks et al.[36] synthesised 3-indole glyoxylic acid (LXXXV) by condensing indole (XVIII) with ethyl oxalate.



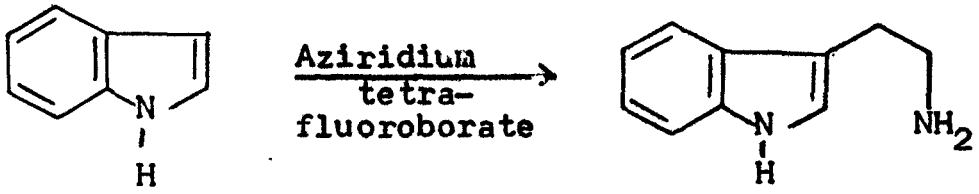
(XVIII) (LXXXV)

Survoror et al.[37] reported a facile method for the synthesis of indole-3-acetic acid (LXXXVI) with chloroacetic acid in presence of KOH.

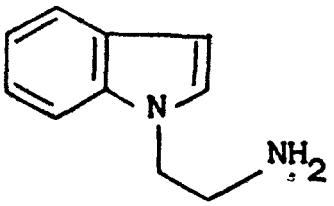


(XVIII) (LXXXVI)

Pfiel and Harder[38] developed a method for 2-amino ethylation at positions 1 and 3 of indole (XVIII) by its reaction with aziridium tetrafluoroborate.

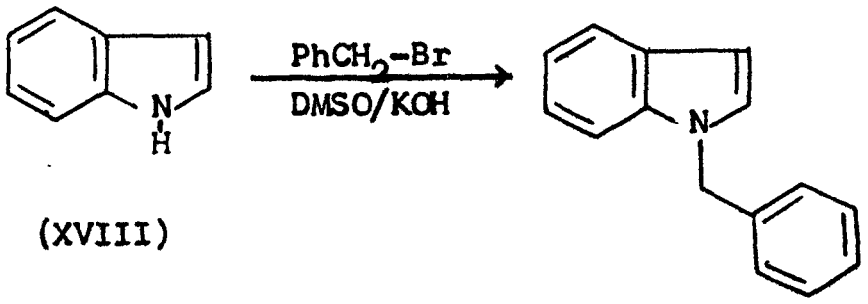


(XVIII) (LXXXVII)



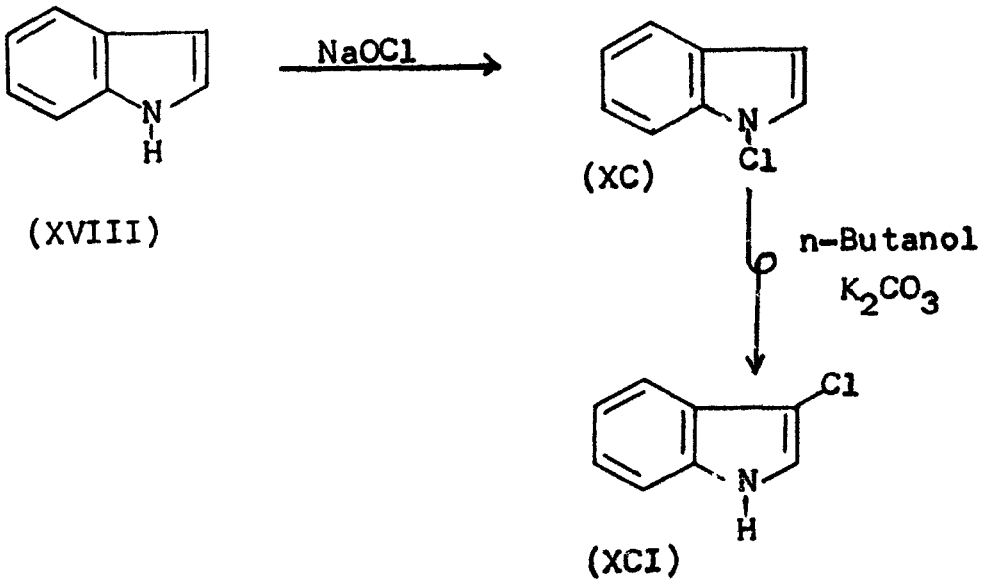
(XXXVIII)

Heaney and Ley[39] prepared 1-benzyl indole (LXXXIX) by the treatment of indole (XVIII) with benzyl bromide in DMSO containing KOH at 25°.

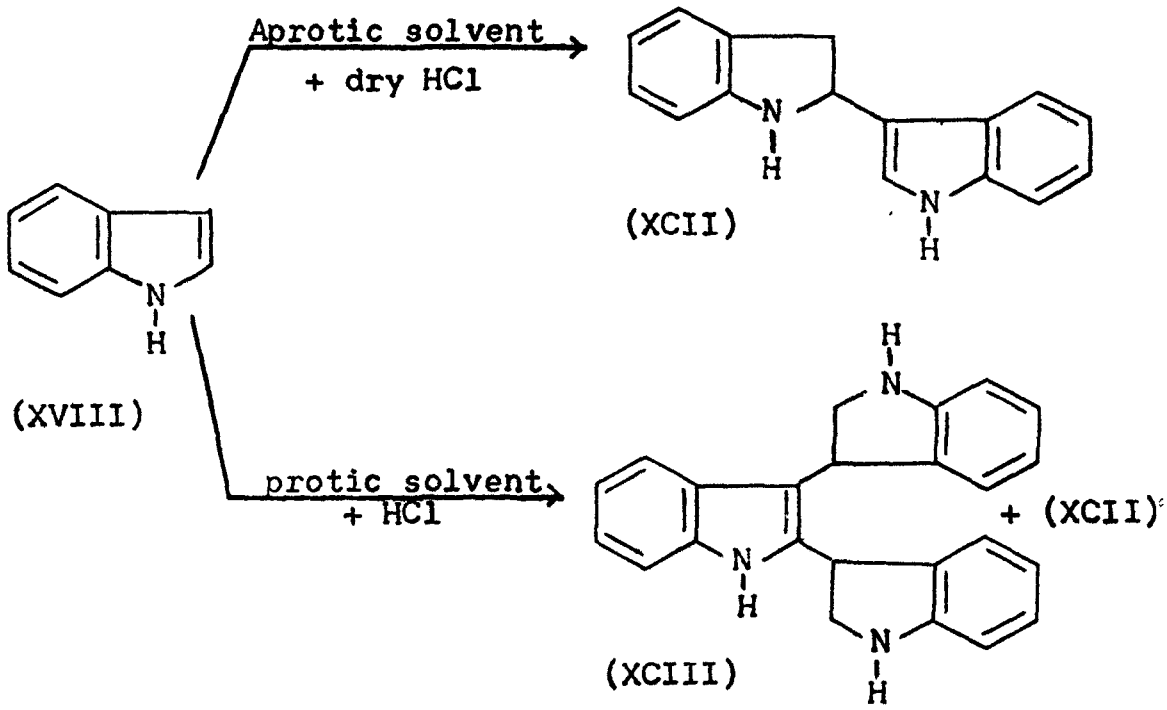


(XVIII) (LXXXIX)

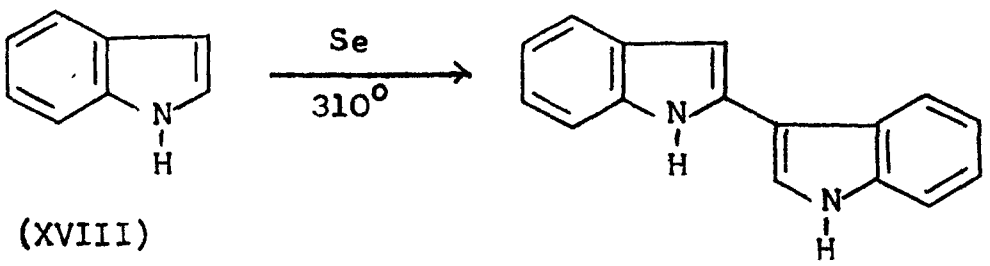
De Rosa[40] treated indole with sodium hypochlorite to give N-chloroindole (XC) which rearranged to give 3-chloroindole (XCI) in n-butyl alcohol containing K_2CO_3.



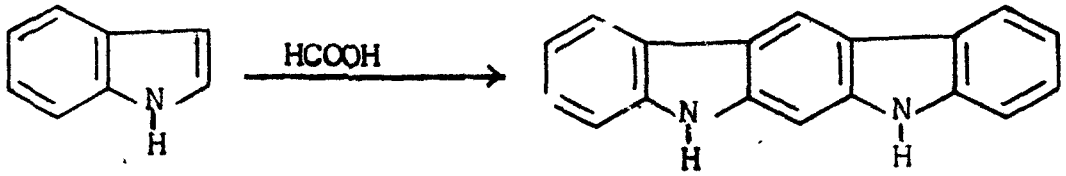
Indole is highly sensitive towards acid[41] and leads to dimerization or trimerization when subjected to react with acid depending on the conditions. Dimer hydrochloride is formed in aprotic solvents with dry HCl,[41,42] whereas aqueous media leads to dimer (XCII) or trimer (XCIII) or both[43]. Due to this, in reactions of indole, the possibility of its dimerization/trimerization are borne into mind and conditions to check it are necessary to achieve some desired modification on a single molecule of indole. Various reactions where the dimerized/trimerized products have been formed are described.



Bergman[44] reported the synthesis of 2,3-diindole (XLIV) by the reaction of indole (XVIII) with selenium at 310°.

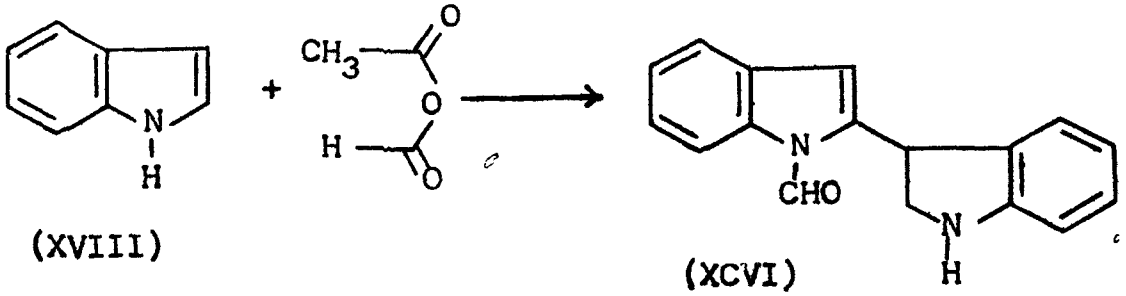


He also carried out the condensation of indole (XVIII) and formic acid in the presence of a strong catalyst and obtained indole (3,2-b) carbazole (XCV) [provided that air, light and an aromatic ketone (sentizer) are present].



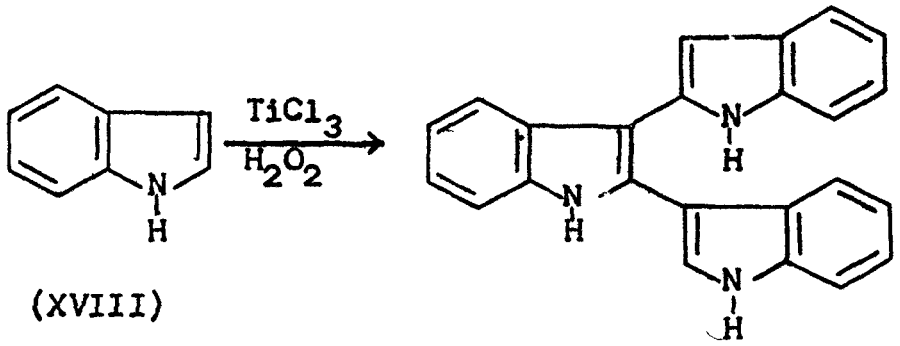
(XVIII) (XCV)

He also demonstrated the reaction of indole (XVIII) with acetic-formic anhydride to give indole (3)-1-formyl indoline (2) (XCVI)[45].



(XVIII) (XCVI)

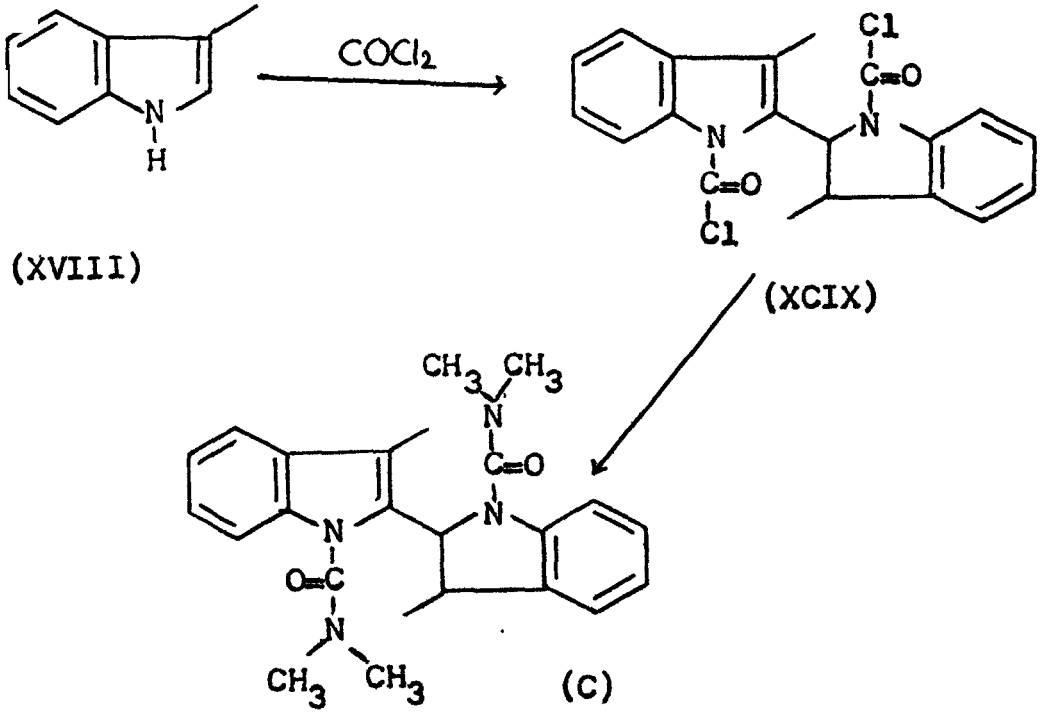
Kaneko et al.[46] prepared triindole (XCVII) by the reaction of indole (XVIII) with $TiCl_3$ in presence of hydrogen peroxide.



(XVIII)

(XCVII)

Bergman et al.[5] have also reported the dimerization of 3-methylindole (XCVIII) during the reaction. They treated 3-methylindole with phosgene in toluene to obtain product (XCIX), isolated as the N,N-dimethylamide derivative (C).



(XVIII)

(XCIX)

(C)

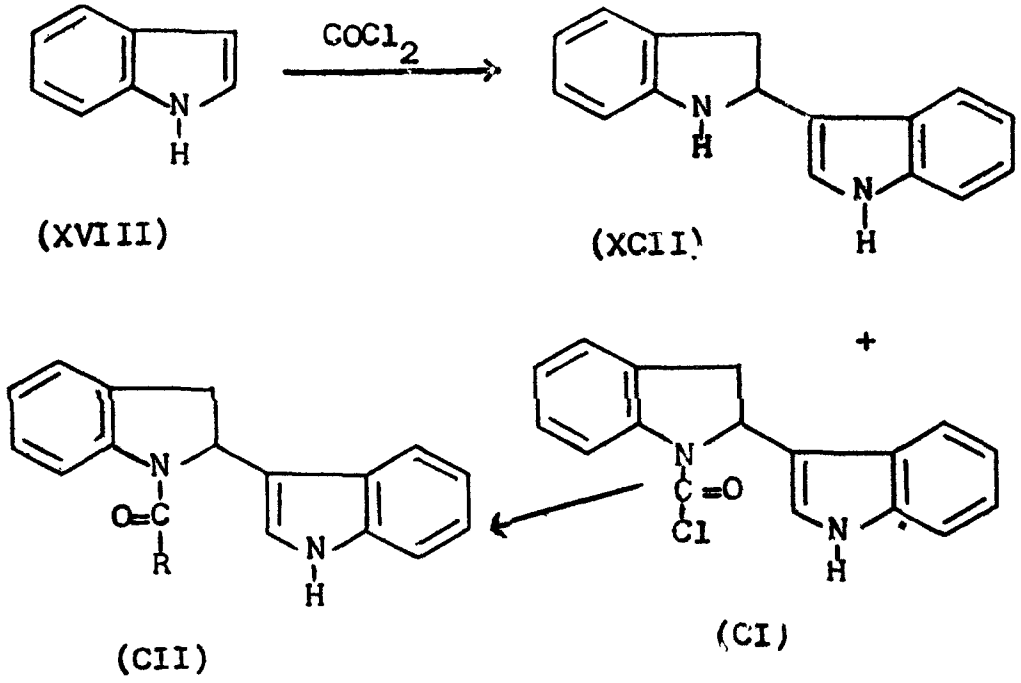
D I S C U S S I O N

The reaction of indole (XVIII) with phosgene was undertaken with a view to obtain dimeric N-carbonyl chloride and its derivatives thereof. Synthesis of these derivatives was our prime motive, because such compounds have been shown to possess various significant properties.

Bergman et al.[5] reported the reaction of the 3-methyl indole (XCVIII) with $COCl_2$ yielding product (XCIX), isolated as the N,N-dimethylamide derivative (C). We, upon a similar treatment of indole (XVIII) with phosgene, however, obtained indole (3)-N-indoline(2)-carbonyl chloride (CI), which is marked by the attachment of the -COCl at the nitrogen of indoline moiety only—the indole moiety remained uneffected. This affords a compound in which the introduction of a suitable reagent furnishes a variety of N-substituted indolinyl indoles (CII a-d).

Reaction of Indole with Phosgene

The reaction of indole (XVIII) with an excess of phosgene below 20° afforded two compounds with melting points of 112° and 132°.



R = (a) $-OCH_3$; (b) $-OC_2H_5$; (c) $-NH-CH_3$; (d) $-NH-CH_2-CH_3$.

Characterization of the Compound, m.p.112°, as Indole Dimer (XCII)

The compound, m.p.112°, showed molecular ion peak at 234 and base peak at m/e 117. The IR spectrum of this compound displayed bands at 3220(C=C-NH), 3185(CH_2-CH-N-H), 1620(C=C) and 740 cm^{-1} (substituted benzene ring). NMR spectrum in conjunction with above data suggested its structure as indolinyl(2)-indole(3) (XCII) by exhibiting a doublet of doublet (J_1=13Hz; J_2=8Hz) at δ 3.00 for 2 protons present at C3 of indoline moiety. A triplet at δ 5.20 with J=8Hz for 1 proton is ascribable for C2 proton adjacent to nitrogen in the same ring. A broad singlet at δ 3.85 (exchangeable with D_2O) was seen due to the NH proton of indoline

moiety. A multiplet centred at δ 7.10 was for 10 protons (8 aromatic+2 vinylic). A broad doublet like signal at δ 7.50 for 1H may be due to the NH proton of the indoline ring. Thus, the compound, m.p.112° has been identified as indole dimer(XCII).

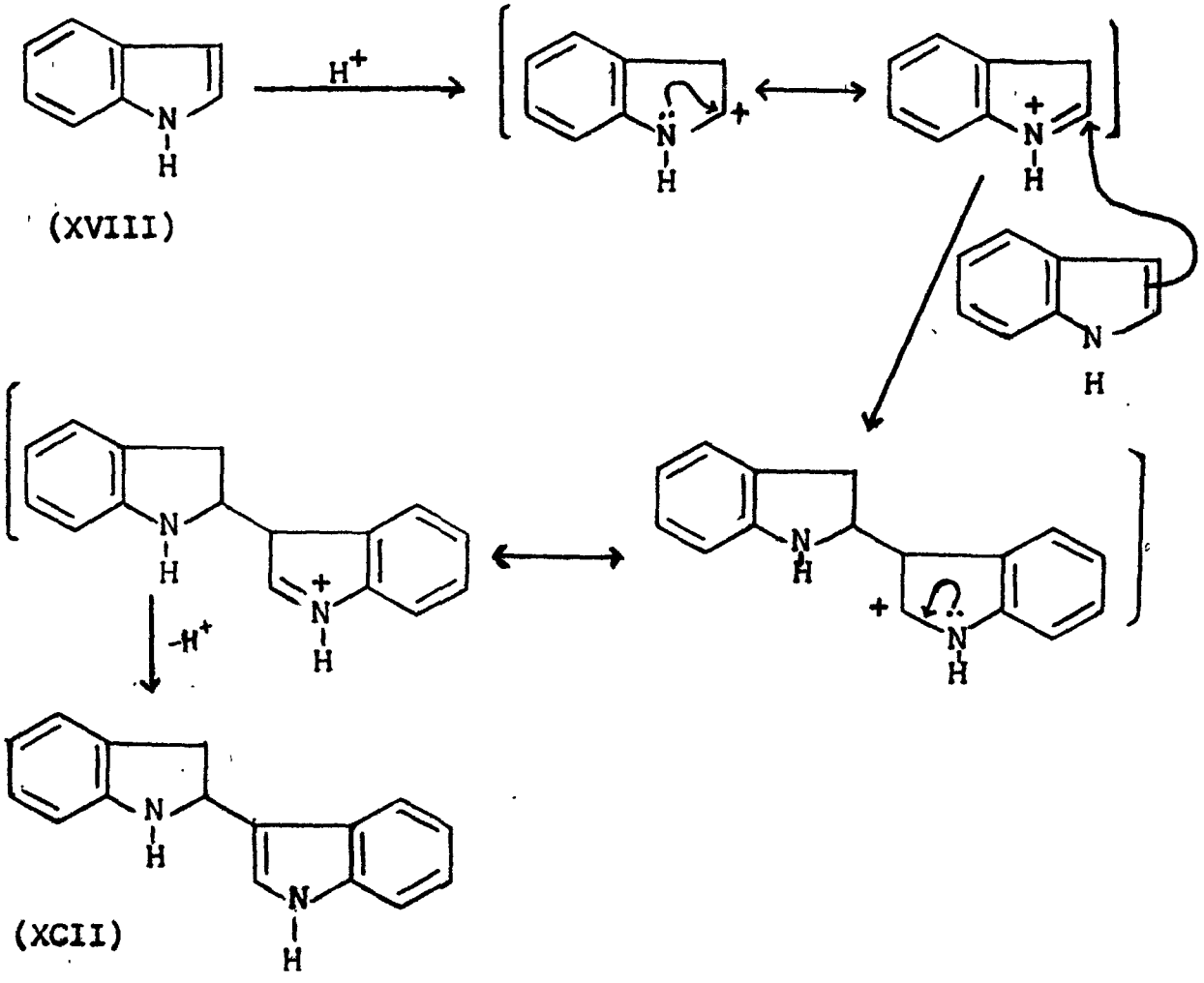
Characterization of the Compound, m.p. 132°, as Indole(3)-N Indoline(2)-Carbonyl Chloride (CI)

The compound, m.p.132°, showing molecular ion peak at 296, 298 (3:1) indicated the formation of a dimer with COCl attached to it. The presence of chlorine was further substantiated by positive Beilstein test for this compound. The fragment m/e 233 clearly suggested the presence of carbonyl chloride moiety in the product. To this, IR spectrum lends further support by exhibiting absorption bands at 3320, 1690 and 820 cm^{-1} for NH, $-N-\overset{O}{\overset{\|}{C}}-Cl$ and C-Cl respectively. NMR spectrum of this compound also supports its assignment as indole(3)-N-indoline(2)-carbonyl chloride. It displayed an uneven doublet of a doublet (J_1= 17Hz; J_2= 2.5Hz) at δ 3.15 integrating for 1H, which is ascribable to one C3-proton. Another doublet of a doublet (J_1= 17Hz; J_2= 9Hz) appearing at δ 3.85 for 1H can be assigned to the other C3-proton. One more doublet of a doublet (J_1= 9Hz; J_2= 2.5Hz) for 1H at δ 5.85 is unmistakably[47] for proton (C2) present on the carbon atom bearing amide and C = C groups. A multiplet for 8H (7 aromatic and 1 vinylic) centred at δ 7.2. A doublet like signal for 1H, characteristic[48] of the aromatic protons in close proximity to C = O at δ 8.00 was seen for C7 aromatic proton. A broad signal (exchangeable with D_2O) for 1H,

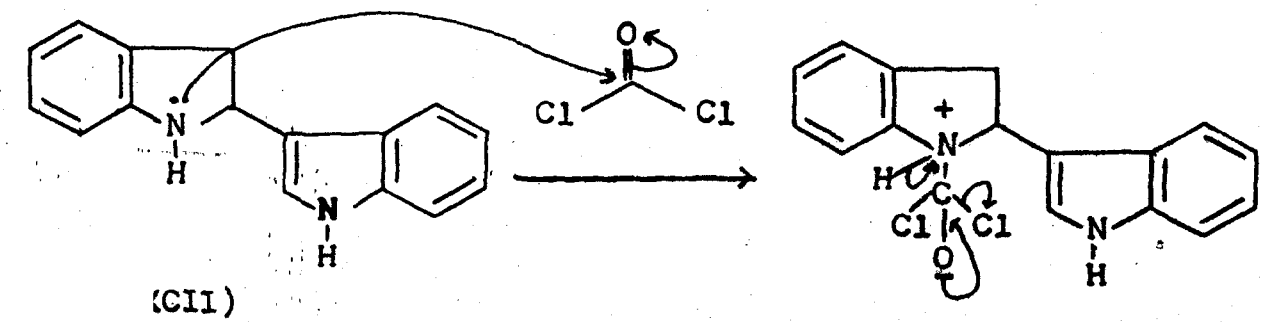
observed at δ 10.03 was due to NH proton of indole moiety of this compound.

On the basis of the foregoing discussion, compound, m.p.132° has been considered as indole(3)-N-indoline(2)-carbonyl chloride (CI). The confirmation of this compound also came from the reaction of indole dimer (XCII) (obtained from dimer hydrochloride) with phosgene furnishing product (CI) exclusively.

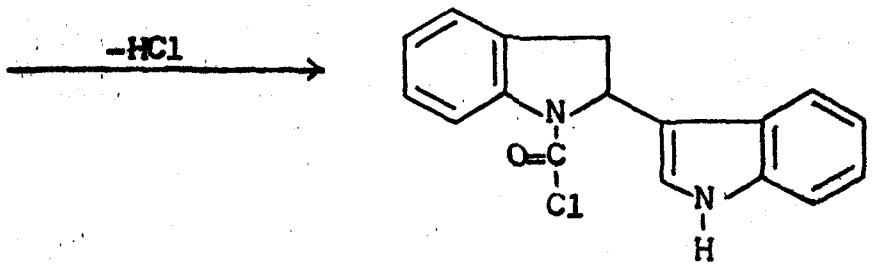
The formation of product (CI) has been rationalized in the light of mechanism for the formation of indole dimer from the reaction of indole and dry HCl, proposed by Hodson and Smith[42].



Position 3 of indole being the richest in electron density is most likely to be attached by an electrophile and consequently the formation of carbonium ion at position 2 which is stabilized by resonance, would simultaneously be attacked by a second molecule of indole resulting in the formation of indole dimer (XCII). This on further reaction with one mole of $COCl_2$, gives the product (CI) in the following manner.

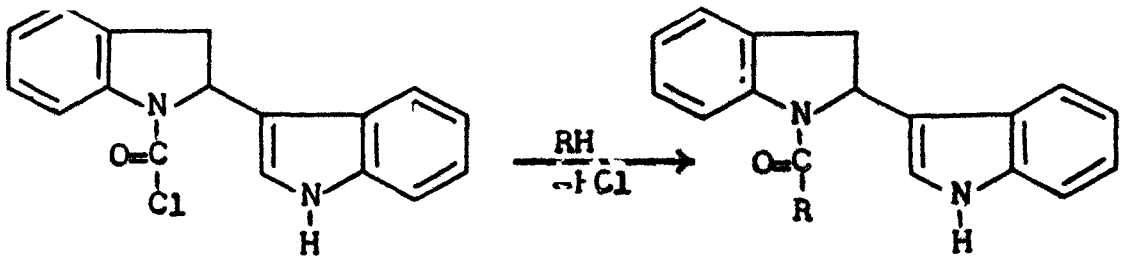


(CII)



(CI)

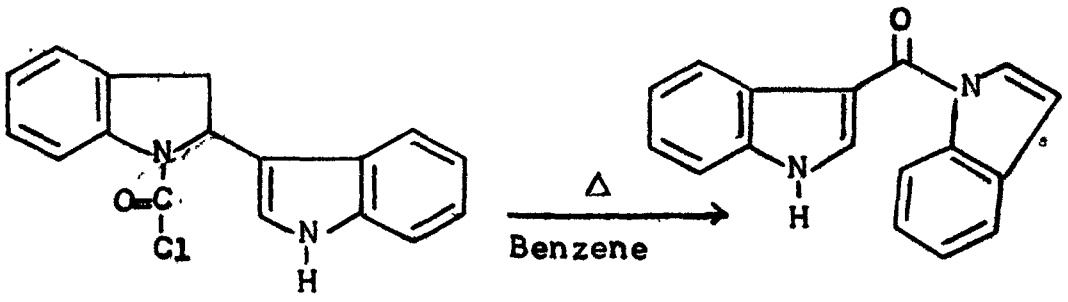
The presence of -COCl moiety in the product has been further supported by its smooth conversion to various derivatives (CII a-d).



(CI) (CII)

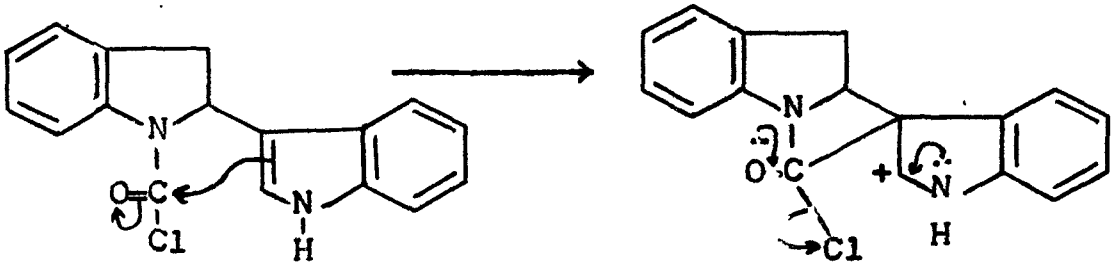
The remarkable feature in the reaction of indole and phosgene is that the -COCl attached at the nitrogen of indoline moiety only — the indole moiety remained uneffected. This is perhaps, due to the electron pair at the nitrogen in the indoline ring being relatively more available to combine with an electron deficient species.

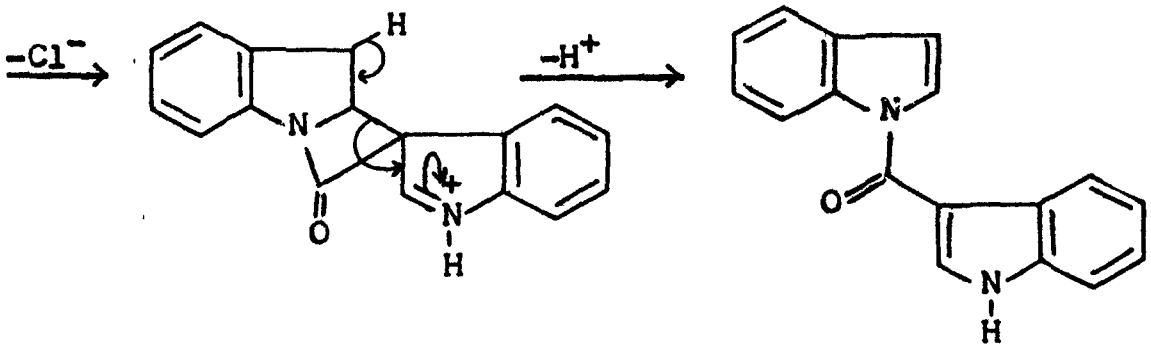
An interesting observation was made when a compound m.p.225° obtained on heating the product (CI) at reflux temperature in dry benzene. The transformed product was identified as 1,3'-carbonyl di-indole (XIV) on the basis of its identity in



(CI) (XIV)

melting point (reported[5], m.p. 227-229°) and spectral data (IR and Mass). The mechanism of its formation, which takes an unusual route, has been proposed underneath.





(XIV)

E X P E R I M E N T A L

All melting points in ^{o}C were taken on Koffler hot block and are uncorrected. Mass spectra were obtained on a JMS-300 Mass spectrometer. IR spectra were determined on a PYE-UNICAM SP3-100 infra-red spectrophotometer. NMR spectra were run in $CDCl_3$/DMSO-d_6 on a Varian A60 instrument using TMS as the internal standard. TLC plates were coated with silica gel G and developed in iodine vapours. Anhydrous sodium sulphate was used as a drying agent.

Preparation of Indolinyl(2)-indole(3) (XCII)

To a solution of indole (5.0 g) in dry benzene (100 ml) was passed dry hydrogen chloride gas (3.0 g) over a period of 30 minutes. The dimer hydrochloride thus precipitated was filtered, washed with dry benzene and air dried. The hydrochloride salt of the dimer was shaken with 10% Na_2CO_3 solution and extracted with ether. The ethereal solution containing the dimer (XCII) was dried over Na_2SO_4 and filtered. Removal of the solvent on a steam bath provided indolinyl(2)-indole(3) (XCII), which was crystallized in petrol-ether mixture (7:3). Yield, 4.0 g; m.p., 112°.

MS: m/e 234(M^+), 117($C_8H_7N^+$). IR(KBr): 3220(C=C-NH), 3185 (CH_2CH-NH), 1620(C=C) and 740 cm^{-1}(substituted benzene). PMR($CDCl_3$): δ 3.00(dd, J_1= 18Hz; J_2= 8Hz, 2H, C3-indoline moiety), 3.85(s, 1H, NH-indoline moiety, exchangeable with D_2O),

5.2(t,J= 8Hz,1H,C2-indoline), 7.8(mc,10H; 8 aromatic+2 vinylic), 7.50 (d,1H,NH-indole ring exchangeable with D_2O).

Reaction of Indole with Phosgene: Indole(3)-N-indoline(2)-carbonyl chloride (CI)

A solution of indole (3.0 g) in benzene (100 ml) was treated with phosgene gas (5.0 g) during 30 minutes with occasional shaking of the reaction mixture at a temperature below 20°C. The progress of the reaction was checked through TLC. After the completion of reaction (2 hours), the precipitated dimer hydrochloride was filtered off in a fuming chamber and the filtrate evaporated under reduced pressure by bubbling the gas through 20% KOH solution or by exposing the filtrate to air in a fuming chamber (heating of the filtrate was avoided in order to get a single product). A crystalline material thus separated was filtered on a buckner funnel and recrystallized from ethyl acetate-benzene (1:3). Yield, 1.8 g; m.p. 132°.

MS: m/e 296, 298(M^+), 261(M^+-Cl), 260(M^+HCl, base peak), 233 (M^+-COCl), 117($C_3H_7N^+$). IR(KBr): 3320(NH), 3080, 3020(C=C-H), 1690(N-C(=O)-Cl), 1590, 1540(C ═══ C), 820 cm^{-1}(C-Cl). PMR($CDCl_3$+ DMSO-d_6): δ 3.15(dd, J_1= 17Hz; J_2= 2.5Hz, 1H, C3-H), 3.85(dd, J_1= 17Hz; J_2= 9Hz, 1H, C3-H), 5.95(dd, J_1= 17Hz; J_2= 2.5Hz, 1H, C2-H), 7.28(m, 8H, 7 aromatic+1 vinylic), 7.55(d, 1H, aromatic H), 10.07(br,s, 1H, NH-indole ring, exchangeable with D_2O).

Reaction of Indole dimer (XCII) with Phosgene: Indole(3)-N-indoline(2)-carbonyl chloride (CI)

A solution of indole dimer (2.0 g) in dry benzene (50 ml) was treated with phosgene gas (2.0 g) during 20 minutes with occasional shaking of the reaction mixture at a temperature below 20°. The progress of the reaction was checked through TLC. After the completion of reaction the solvent was evaporated under reduced pressure or by exposing the filtrate to air in a fuming chamber (heating of the filtrate was avoided in order to get a single product). A crystalline material, thus separated was filtered on a buckner funnel and recrystallized from ethyl acetate-benzene (1:3). Yield, 1.3 g; m.p. 132°.

This compound was found to be identical with the authentic sample (CI) in all respects (TLC, m.p., m.m.p. and IR).

1,3'-Carbonyl di-indole (XIV)

Compound (CI) (2.0 g) in benzene (100 ml) was heated at reflux temperature for 2 hours. A change in colour from colourless to yellow was observed. This solution was then washed with water, and extracted by ethyl acetate. Removal of the solvent provided solid residue which was chromatographed over silica gel. Elution with benzene-ethyl acetate (20:1) gave compound (XIV) which was crystallized from methanol. Yield, 1.1 g; m.p. 225° (Reported m.p. 227-229°).

MS: m/e 261(M^+), 117($C_8H_7N^+$). IR(KBr): 3320(NH), 3080, 3020 (C=C-H), 1680(N-C-N), 1590, 1540 cm^{-1}(C = C). PMR($CDCl_3$ + $DMSOd_6$): δ 7.3(mc, 10H, 7 aromatic + 3 vinylic), 7.6(d, 1H, aromatic proton), 10.7(br,s, 1H, NH-indole ring, exchangeable with D_2O).

N-Carbomethoxyindoline(2)-indole(3) (CII)

Compound (CI) (1.0 g) was treated at room temperature with methanol (50 ml,80%) in the presence of $Ba(OH)_2$ (1.0 g) for a period of 2 hours with occasional shaking. After the completion of reaction (progress of the reaction was checked through TLC), solvent was reduced to 10 ml and the contents poured into cold water. It was then extracted with ether and the ethereal layer washed twice with water, dried over anhydrous sodium sulphate and the dessicant removed. Removal of the solvent gave an oily residue which was crystallized from methanol. Yield, 0.80 g; m.p. 173°.

MS: m/e 292(M^+), 261(M^+-OCH_3), 233($M^+-OCOCH_3$), 117(base peak). IR: 3300(NH), 3080, 3020(C=C-H), 1675(N-C(=O)-O-CH_3), 1590, 1540 (C = C), 1120, 1050(C-O), 750 cm^{-1}(substituted benzene). PMR: δ 3.15(dd, J_1= 17Hz; J_2= 2.5Hz, 1H, C3-H), 3.75(dd, J_1= 17Hz; J_2= 9Hz, 1H, C2-H), 3.67(s, 3H, -C(=O)-OCH_3), 5.80(dd, J_1= 9Hz; J_2= 2.5Hz, 1H, C2-H), 7.28(mc, 8H, 7 aromatic+1 vinylic), 7.55 (d, 1H, C7-H), 10.07(br,s, 1H, exchangeable with D_2O, NH-indole ring).

N-Carboethoxyindoline(2)-indole(3) (CII-b)

A mixture of (CI) (1.0 g), ethyl alcohol (50 ml, 80%) was stirred on a magnetic stirrer at room temperature in the presence of $Ba(OH)_2$ (1.0 g) for a period of 2 hours (progress of the reaction was checked through TLC). After the reaction was complete, solvent reduced to 10 ml and the contents poured into cold water. It was then extracted with ether, the ethereal layer washed twice with water, dried over anhydrous sodium sulphate and the dessicant removed. Removal of the solvent gave an oily residue, which was purified on a silica gel column. Crystallization from ethanol gave (CII-b). Yield, 0.65 g; m.p. 136°.

MS: m/e 306(M^+), 261($M^+-OC_2H_5$), 233($M^+-\overset{O}{\overset{\|}{C}}-OC_2H_5$), 117($C_5H_8N^+$). IR: 3290(NH), 3068, 3015(C=C-H), 1670(N-$\overset{O}{\overset{\|}{C}}$-$OC_2H_5$), 740 cm^{-1} (substituted benzene). PMR: δ 1.17(t, 3H, N-$\overset{O}{\overset{\|}{C}}$-$OCH_2$-$\underline{CH_3}$), 3.07 (dd, J_1= 16Hz; J_2= 3Hz, 1H, C3-H), 3.70(dd, J_1= 16Hz; J_2= 10Hz, 1H, C3-H), 4.13(q, 2H, N-$\overset{O}{\overset{\|}{C}}$-$\underline{CH_2}$-$CH_3$), 5.77(dd, J_1= 10Hz; J_2= 3Hz, 1H, C2-H), 7.08(mc, 8H, 7 aromatic+1 vinylic), 7.83(d like, 1H, C7-H aromatic), 8.83(br,s, exchangeable with D_2O, NH indole ring).

N,N-Methylamidoindoline(2)-indole(3) (CII-c)

A solution of (CI) (1.0 g) in THF (25 ml) was mixed with methyl amine (5 ml) and kept at room temperature for

2 hours, when the reaction completed. Excess methyl amine was then removed under reduced pressure and the contents poured into cold water. The compound thus separated was filtered on a buckner funnel. This on crystallization (from methanol) gave (CII-c). Yield, 0.75 g; m.p. 183°.

MS: m/e 291(M^+), 261, 233, 117. IR(KBr): 3420(NH-CH_3), 3300 (NH-indole ring), 3050, 3030(C=C-H), 1650(N-C(=O)-N), 1350(C-N), 760 cm^{-1}(substituted benzene). PMR: δ 2.67(s, 3H, N-C(=O)-N-CH_3), 3.06(dd, J_1= 17Hz; J_2= 3Hz, 1H, C3-H), 3.78(dd, J_1= 17Hz; J_2= 10Hz, 1H, C3-H), 5.50(dd, J_1= 10Hz; J_2= 3Hz, 1H, C2-H), 7.20 (mc, 8H, 7 aromatic+1 vinylic), 8.06(d, 1H, C7-H aromatic), 9.5 (br,s, exchangeable with D_2O, NH-indole ring).

N,N-Ethylamidoindoline(2)-indole(3) (CII-d)

Reaction of compound (CI) (1.0 g) in THF (25 ml) with ethylamine (5 ml) was carried out in the usual manner. After the completion of the reaction (progress of the reaction was checked through TLC), excess solvent was removed under reduced pressure and the contents poured into water. The compound thus separated was collected on a buckner funnel. This on crystallization (from methanol) gave (CII-d). Yield, 0.70 g; m.p.183°.

MS: m/e 305(M^+), 261, 233, 117. IR(KBr): 3475(NH), 3280(NH-indole ring), 1648 cm^{-1}(N-C(=O)-N-CH_2-CH_3). PMR: δ 1.12(t, 3H, N-C(=O)-N-CH_2-CH_3), 3.10(dd, J_1= 15.5Hz; J_2= 3Hz, 1H, C3-H), 3.68

(dd, J_1= 15.5Hz; J_2= 9Hz, 1H, C3-H), 3.98(q, 2H, NH-$\underline{CH_2}$-CH_3), 5.73(dd, J_1= 9Hz; J_2= 3Hz, 1H, C2-H), 7.13(mc, 8H, 7 aromatic + 1 vinylic), 7.90(dist. d, 1H, C7-H), 9.23(br,s, 1H, exchangeable with D_2O, NH-indole ring).

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